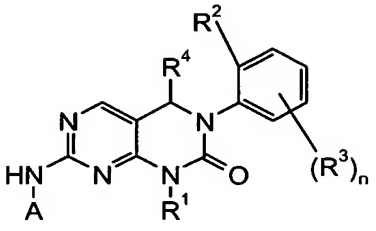
Claims

1. A compound of formula I



I

wherein

R^1 represents hydrogen or

alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl, each of which may be optionally substituted with halogen, hydroxy, cyano, nitro, amino, acylamino, alkyl, alkoxy, alkoxyalkyl, $-CONH_2$, $-SO_2NH_2$, $-S(O)_m$-alkyl, -NH-alkyl, $-N(alkyl)_2$, -CONH(alkyl), $CON(alkyl)_2$, $-SO_2NH(alkyl)$, $-SO_2N(alkyl)_2$;

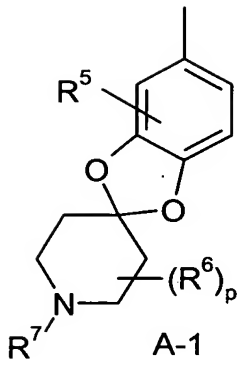
R^2 represents halogen, cyano or CF_3;

R^3 each R^3 is independently selected from halogen, hydroxy, cyano, nitro, amino, acylamino, $-CONH_2$, $-SO_2NH_2$, $-S(O)_m$-alkyl, -NH-alkyl, $-N(alkyl)_2$, -CONH(alkyl), $-CON(alkyl)_2$, $-SO_2NH(alkyl)$, $-SO_2N(alkyl)_2$, or

alkyl, alkoxy or alkoxyalkyl, each of which may be optionally substituted with halogen, hydroxy, cyano, nitro, amino, acylamino, alkyl, alkoxy, alkoxyalkyl, $-CONH_2$, $-SO_2NH_2$, $-S(O)_m$-alkyl, -NH-alkyl, $-N(alkyl)_2$, -CONH(alkyl), $CON(alkyl)_2$, $-SO_2NH(alkyl)$, $-SO_2N(alkyl)_2$;

R^4 represents hydrogen, alkyl, alkoxy or cyano;

A is selected from the group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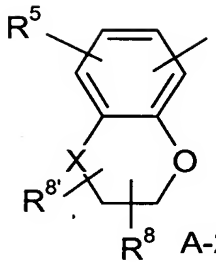
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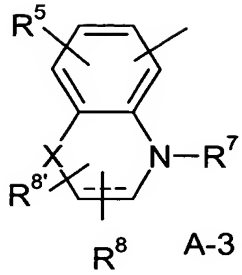
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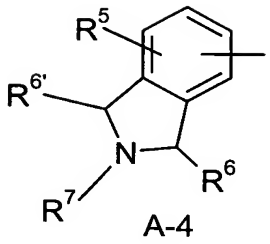
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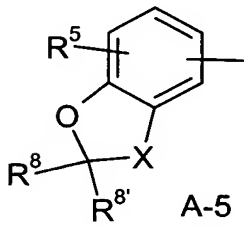
A-5

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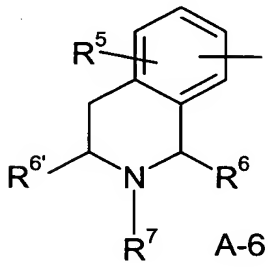

A-6

,

R^5 is hydrogen, halogen, hydroxy, cyano, amino, acylamino, alkyl, alkoxy, alkoxyalkyl, $-CONH_2$, $-SO_2NH_2$, $-S(O)_m$-alkyl, -NH-alkyl, $-N(alkyl)_2$, -CONH(alkyl), $-CON(alkyl)_2$, $-SO_2NH(alkyl)$ or $-SO_2N(alkyl)_2$;

R^6, $R^{6'}$ are each independently selected from hydrogen, alkyl or oxo;

R^7 is hydrogen, acyl, alkoxycarbonyl, alkoxyalkyl, alkyl or alkyl substituted with hydroxy, cyano,$-S(O)_m$-alkyl, amino, -NH-alkyl or $-N(alkyl)_2$;

R^8, $R^{8'}$ are each independently selected from hydrogen, oxo, alkoxy, alkoxyalkyl, alkyl or alkyl substituted with hydrogen, hydroxy, cyano, pyrrolidin-1-yl, morpholino, piperazin-1-yl, 4-alkyl-piperazin-1-yl, piperidin-1-yl, $-S(O)_m$-alkyl, or a group $NR^9R^{9'}$, provided that when either R^8 or $R^{8'}$ represent an oxo group, this oxo group is not adjacent to an $S(O)_m$ group;

R^9 and $R^{9'}$ are each independently selected from hydrogen, alkyl or cycloalkyl;

X is oxygen or $S(O)_m$;

the dashed line is an optional second chemical bond;

n is 0, 1 or 2;

m is 0, 1 or 2; and

p is 0, 1 or 2;

or a pharmaceutically acceptable salt or N-oxides thereof.

2. A compound according to claim 1,

wherein

R^1 represents hydrogen or

alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl, or heteroarylalkyl, each of which may be optionally substituted with halogen, hydroxy, cyano, nitro, amino, acylamino, alkyl, alkoxy, alkoxyalkyl, $-CONH_2$, $-SO_2NH_2$, $-S(O)_m$-alkyl, -NH-alkyl, $-N(alkyl)_2$, -CONH(alkyl), $CON(alkyl)_2$, $-SO_2NH(alkyl)$, or $-SO_2N(alkyl)_2$;

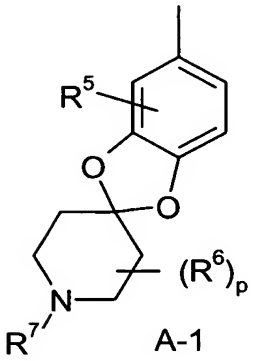
R^2 represents halogen, cyano or CF_3;

R^3 each R^3 is independently selected from halogen, hydroxy, cyano, nitro, amino, acylamino, $-CONH_2$, $-SO_2NH_2$, $-S(O)_m$-alkyl, -NH-alkyl, $-N(alkyl)_2$, -CONH(alkyl), $-CON(alkyl)_2$, $-SO_2NH(alkyl)$, $-SO_2N(alkyl)_2$, or

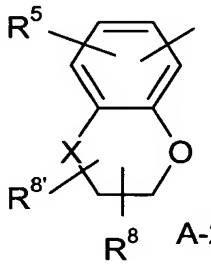
alkyl, alkoxy or alkoxyalkyl, each of which may be optionally substituted with halogen, hydroxy, cyano, nitro, amino, acylamino, alkyl, alkoxy, alkoxyalkyl, $-CONH_2$, $-SO_2NH_2$, $-S(O)_m$-alkyl, -NH-alkyl, $-N(alkyl)_2$, -CONH(alkyl), $CON(alkyl)_2$, $-SO_2NH(alkyl)$, or $-SO_2N(alkyl)_2$;

R^4 represents hydrogen, alkyl, alkoxy or cyano;

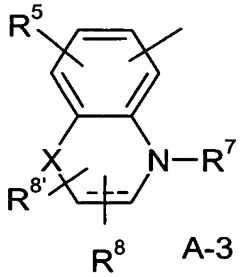
A is selected from



A-1



A-2



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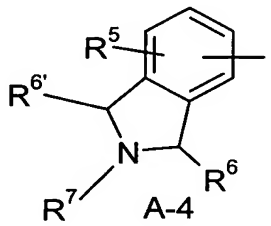
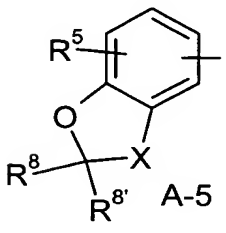
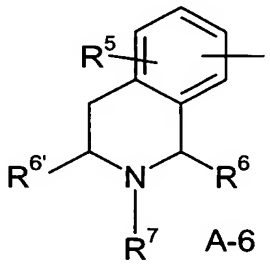


A-4



A-5

or



A-6

,

R^5 is hydrogen, halogen, hydroxy, cyano, amino, acylamino, alkyl, alkoxy, alkoxyalkyl, $-CONH_2$, $-SO_2NH_2$, $-S(O)_m$-alkyl, -NH-alkyl, $-N(alkyl)_2$, -CONH(alkyl), $-CON(alkyl)_2$, $-SO_2NH(alkyl)$ or $-SO_2N(alkyl)_2$;

R^6, $R^{6'}$ are each independently selected from hydrogen, alkyl or oxo;

R^7 is hydrogen, acyl, alkoxycarbonyl, alkoxyalkyl, alkyl or alkyl substituted with hydroxy, cyano,$-S(O)_m$-alkyl, amino, -NH-alkyl or $-N(alkyl)_2$;

R^8, $R^{8'}$ are each independently selected from hydrogen, oxo, alkoxy, alkoxyalkyl, alkyl or alkyl substituted with hydrogen, cyano, pyrrolidin-1-yl, morpholino, piperazin-1-yl, 4-alkyl-piperazin-1-yl, piperidin-1-yl, $-S(O)_m$-alkyl, or a group $NR^9R^{9'}$,provided that when either R^8 or $R^{8'}$ represent an oxo group, this oxo group is not adjacent to an $S(O)_m$ group;

R^9 and $R^{9'}$ are each independently selected from hydrogen, alkyl or cycloalkyl;

X is oxygen or $S(O)_m$;

the dashed line is an optional second chemical bond;

n is 0, 1 or 2;

m is 0, 1 or 2; and

p is 0, 1 or 2;

or a pharmaceutically acceptable salt or N-oxides thereof.

3. The compound of claim 2 wherein R^2 is bromine and n = 0.

4. The compound of claim 2 wherein n is 1 and R^2 and R^3 are each independently selected from fluorine, chlorine, bromine or iodine.

5. The compound of claim 4 wherein R^2 is bromine and R^3 is fluorine.

6. The compound of claim 5 wherein the R^3 is at the 6-position of the phenyl ring.

7. The compound of claim 4 wherein R^2 and R^3 are both chlorine.

8. The compound of claim 2,

wherein

A is selected from A-1, A-2, A-3, A-4, A-5 or A-6;

R^1 is alkyl or aryl, each of which may be optionally substituted with halogen, hydroxy, cyano, nitro, amino, acylamino, alkyl, alkoxy, alkoxyalkyl, $-CONH_2$, $-SO_2NH_2$, $-S(O)_m$-alkyl, -NH-alkyl, $-N(alkyl)_2$, -CONH(alkyl), $CON(alkyl)_2$, $-SO_2NH(alkyl)$, or $-SO_2N(alkyl)_2$;

R^2 is halogen or cyano;

R^3 each R^3 is independently selected from halogen;

n is 0 or 1;

m is 0, 1 or 2;

R^5 is hydrogen; and

R^4 hydrogen or methyl; or

a pharmaceutically acceptable salt thereof.

9. The compound according to claim 8 selected from

7-(Benzo[1,3]dioxol-5-ylamino)-3-(2,4-dichloro-phenyl)-1-(4-methoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one; and

2-[7-(4,4-Dioxo-3,4-dihydro-2H-4lambda*6*-benzo[1,4]oxathiin-6-ylamino)-1-methyl-2-oxo-1,4-dihydro-2H-pyrimido[4,5-d]pyrimidin-3-yl]-benzonitrile.

10. The compound of claim 2 wherein

A is A-1;

R^5 is hydrogen;

p is 0;

R^1 is alkyl;

R^2 is halogen;

R^3 is halogen;

n is 0 or 1; and

R^4 is hydrogen;

or a pharmaceutically acceptable salt thereof.

11. The compound according to claim 10 which is selected from 3-(2-bromo-phenyl)-3,4-dihydro-7-(1'-acetyl-spiro[1,3-benzodioxolo-2,4'-piperidine]-5-yl)amino-1-methyl-pyrimido[4,5-d]pyrimidin-2(1H)-one,
3-(2-bromo-phenyl)-3,4-dihydro-7-(1'-ethoxycarbonyl-spiro[1,3-benzodioxolo-2,4'-piperidine]-5-yl)amino-1-methyl-pyrimido[4,5-d]pyrimidin-2(1H)-one,
3-(2-bromo-6-fluorophenyl)-3,4-dihydro-7-(1'-acetyl-spiro[1,3-benzodioxolo-2,4'-piperidine]-5-yl)amino-1-methyl-pyrimido[4,5-d]pyrimidin-2(1H)-one,
3-(2-bromo-6-fluorophenyl)-3,4-dihydro-7-(1'-ethoxycarbonyl-spiro[1,3-benzodioxolo-2,4'-piperidine]-5-yl)amino-1-methyl-pyrimido[4,5-d]pyrimidin-2(1H)-one,
3-(2-bromo-phenyl)-3,4-dihydro-7-(1'-ethyl-spiro[1,3-benzodioxolo-2,4'-piperidine]-5-yl)amino-1-methyl-pyrimido[4,5-d]pyrimidin-2(1H)-one,
3-(2-bromo-phenyl)-3,4-dihydro-7-(1'-(2-methoxyethyl)-spiro[1,3-benzodioxolo-2,4'-piperidine]-5-yl)amino-1-methyl-pyrimido[4,5-d]pyrimidin-2(1H)-one, and
3-(2-bromo-6-fluorophenyl)-3,4-dihydro-7-(1'-(2-methoxyethyl)-spiro[1,3-benzodioxolo-2,4'-piperidine]-5-yl)amino-1-methyl-pyrimido[4,5-d]pyrimidin-2(1H)-one.

12. The compound according to claim 10 which is selected from 3-(2-bromo-phenyl)-3,4-dihydro-7-(spiro[1,3-benzodioxolo-2,4'-piperidine]-5-yl)amino-1-methyl-pyrimido[4,5-d]pyrimidin-2(1H)-one,
3-(2-bromo-phenyl)-3,4-dihydro-7-(1'-methyl-spiro[1,3-benzodioxolo-2,4'-piperidine]-5-yl)amino-1-methyl-pyrimido[4,5-d]pyrimidin-2(1H)-one,
3-(2-bromo-6-fluoro-phenyl)-3,4-dihydro-7-(spiro[1,3-benzodioxolo-2,4'-piperidine]-5-yl)amino-1-methyl-pyrimido[4,5-d]pyrimidin-2(1H)-one,
3-(2-bromo-6-fluoro-phenyl)-3,4-dihydro-7-(1'-methyl-spiro[1,3-benzodioxolo-2,4'-piperidine]-5-yl)amino-1-methyl-pyrimido[4,5-d]pyrimidin-2(1H)-one,
3-(2-bromo-phenyl)-3,4-dihydro-7-(1'-cyanomethyl-spiro[1,3-benzodioxolo-2,4'-piperidine]-5-yl)amino-1-methyl-pyrimido[4,5-d]pyrimidin-2(1H)-one, and
3-(2-bromo-5-methoxyphenyl)-3,4-dihydro-7-(spiro[1,3-benzodioxolo-2,4'-piperidine]-5-yl)amino-1-methyl-pyrimido[4,5-d]pyrimidin-2(1H)-one.

13. The compound according to claim 2 wherein

A is a group A-2;

R^5 is hydrogen;

X is oxygen;

R^8, $R^{8'}$ are each independently selected from hydrogen or alkyl that optionally may be substituted with cyano, pyrrolidin-1-yl, morpholino, piperazin-1-yl, 4-alkyl-piperazin-1-yl, piperidin-1-yl, $-S(O)_m$-alkyl, or a group $NR^9R^{9'}$;

R^9 and $R^{9'}$ are each independently selected from hydrogen, alkyl or cycloalkyl;

R^1 is alkyl;

R^2 is halogen;

R^3 is halogen;

n is 0 or 1; and

R^4 is hydrogen;

or a pharmaceutically acceptable salt thereof.

14. The compound according to claim 13, which is selected from 3-(2-bromo-phenyl)-7-(2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-phenyl)-1-methyl-7-(2-pyrrolidin-1-ylmethyl-2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-phenyl)-1-methyl-7-(3-pyrrolidin-1-ylmethyl-2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-phenyl)-7-(2-dimethylaminomethyl-2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-6-fluoro-phenyl)-7-(2-dimethylaminomethyl-2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-phenyl)-7-(3-dimethylaminomethyl-2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-6-fluoro-phenyl)-7-(3-dimethylaminomethyl-2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-phenyl)-7-(2-cyclopropylaminomethyl-2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-phenyl)-1-methyl-7-(2-morpholin-4-ylmethyl-2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,

3-(2-bromo-phenyl)-1-methyl-7-(3-morpholin-4-ylmethyl-2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one, 3-(2-bromo-6-fluoro-phenyl)-1-methyl-7-(3-morpholin-4-ylmethyl-2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one, and 3-(2-bromo-6-fluoro-phenyl)-1-methyl-7-(3-pyrrolidin-1-ylmethyl-2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one.

15. The compound according to claim 1 wherein

A is a group A-2;

R^5 is hydrogen;

X is oxygen;

R^8 is hydrogen

$R^{8'}$ is alkyl substituted with hydroxy;

R^1 is alkyl;

R^2 is halogen;

R^3 is halogen;

n is 0 or 1; and

R^4 is hydrogen;

or a pharmaceutically acceptable salt thereof.

16. The compound according to claim 15, which is selected from 3-(2-bromo-phenyl)-7-(2-hydroxymethyl-2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one, 3-(2-bromo-phenyl)-7-(3-hydroxymethyl-2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one, 3-(2-bromo-6-fluoro-phenyl)-7-(3-hydroxymethyl-2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one, and 3-(2-bromo-6-fluoro-phenyl)-7-(2-hydroxymethyl-2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one.

17. The compound of claim 2 wherein

A is A-2;

R^5 is hydrogen;

X is $S(O)_m$;

m is 0, 1 or 2;

R^8, $R^{8'}$ are hydrogen;

R^1 is alkyl;

R^2 is halogen;

R^3 is halogen;

n is 0 or 1; and

R^4 is hydrogen;

or a pharmaceutically acceptable salt thereof.

18. The compound according to claim 17, which is selected from 3-(2-bromo-phenyl)-7-(2,3-dihydro-benzo[1,4]oxathiin-7-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-phenyl)-7-(4,4-dioxo-3,4-dihydro-2H-4lambda*6*-benzo[1,4]oxathiin-7-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-6-fluoro-phenyl)-7-(4,4-dioxo-3,4-dihydro-2H-4lambda*6*-benzo[1,4]oxathiin-6-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one, and
3-(2-bromo-phenyl)-7-(4,4-dioxo-3,4-dihydro-2H-4lambda*6*-benzo[1,4]oxathiin-6-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one.

19. The compound of claim 2 wherein

A is A-3;

R^5 is hydrogen;

R^7 is hydrogen or alkyl;

X is $S(O)_m$;

m is 0, 1 or 2;

R^8, $R^{8'}$ are each independently selected from hydrogen, oxo or alkoxy,

provided that when one of R^8, $R^{8'}$ is oxo the dashed line is absent, and provided further that when R^8 and $R^{8'}$ are selected from hydrogen or alkoxy the dashed line may represent an additional bond to form a double bond;

R^1 is alkyl;

R^2 is halogen;

R^3 is halogen;

n is 0 or 1; and

R^4 is hydrogen;
or a pharmaceutically acceptable salt thereof.

20. The compound according to claim 19 which is selected from

3-(2-bromo-phenyl)-1-methyl-7-(3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-7-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-phenyl)-1-methyl-7-(4-methyl-3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-7-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-phenyl)-1-methyl-7-(4-methyl-1,3-dioxo-1,2,3,4-tetrahydro-1lambda*4*-benzo[1,4]thiazin-7-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-phenyl)-1-methyl-7-(4-methyl-3,4-dihydro-2H-benzo[1,4]thiazin-7-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-phenyl)-1-methyl-7-(3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-6-fluoro-phenyl)-1-methyl-7-(4-methyl-3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-7-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one, and
3-(2-bromo-6-fluoro-phenyl)-1-methyl-7-(3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one.

21. The compound according to claim 19 which is selected from

3-(2-bromo-phenyl)-1-methyl-7-(4-methyl-3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-phenyl)-7-(3-methoxy-4-methyl-1-oxo-1,4-dihydro-1lambda*4*-benzo[1,4]thiazin-7-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-6-fluoro-phenyl)-1-methyl-7-(4-methyl-3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-6-fluoro-phenyl)-1-methyl-7-(4-methyl-1,1-dioxo-1,2,3,4-tetrahydro-1lambda*6*-benzo[1,4]thiazin-7-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-bromo-phenyl)-1-methyl-7-(4-methyl-1,1-dioxo-1,2,3,4-tetrahydro-1lambda*6*-benzo[1,4]thiazin-7-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,

3-(2-bromo-phenyl)-1-methyl-7-(4-methyl-1,1,3-trioxo-1,2,3,4-tetrahydro-1lambda*6*-benzo[1,4]thiazin-7-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one, and 3-(2-bromo-6-fluoro-phenyl)-1-methyl-7-(4-methyl-1,1,3-trioxo-1,2,3,4-tetrahydro-1lambda*6*-benzo[1,4]thiazin-7-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one.

22. The compound of claim 2, wherein

A is A-4;

R^5 is hydrogen;

R^6, $R^{6'}$ are each independently selected from hydrogen or oxo;

R^7 is hydrogen or alkyl that optionally may be substituted with hydroxy, cyano,-$S(O)_m$-alkyl, amino, -NH-alkyl or -$N(alkyl)_2$;

R^1 is alkyl;

R^2 is halogen;

R^3 is halogen;

n is 0 or 1;

m is 0, 1 or 2;

R^4 is hydrogen;

or a pharmaceutically acceptable salts thereof.

23. The compound according to claim 22 which is selected from 5-[6-(2-bromo-phenyl)-8-methyl-7-oxo-5,6,7,8-tetrahydro-pyrimido[4,5-d]pyrimidin-2-ylamino]-2-methyl-isoindole-1,3-dione,
3-(2-bromo-phenyl)-1-methyl-7-(2-methyl-2,3-dihydro-1H-isoindol-5-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one; hydrochloride salt,
5-[6-(2-bromo-phenyl)-8-methyl-7-oxo-5,6,7,8-tetrahydro-pyrimido[4,5-d]pyrimidin-2-ylamino]-isoindole-1,3-dione,
5-[6-(2-bromo-6-fluoro-phenyl)-8-methyl-7-oxo-5,6,7,8-tetrahydro-pyrimido[4,5-d]pyrimidin-2-ylamino]-2-methyl-isoindole-1,3-dione, and
3-(2-bromo-6-fluoro-phenyl)-7-[2-(2-hydroxy-1,1-dimethyl-ethyl)-2,3-dihydro-1H-isoindol-5-ylamino]-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one; hydrochloride.

24. The compound of claim 2, wherein

A is A-5;

R^5 is hydrogen;

X is oxygen;

R^8, $R^{8'}$ are each independently selected from hydrogen or alkyl;

R^1 is alkyl;

R^2 is halogen;

R^3 is halogen;

n is 0 or 1; and

R^4 is hydrogen; or

a pharmaceutically acceptable salt thereof.

25. The compound according to claim 24 which is 7-(benzo[1,3]dioxol-5-ylamino)-3-(2-bromo-phenyl)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one.

26. A compound of claim 2, wherein

A is A-5';

R^5 is hydrogen;

X is $S(O)_m$;

m is 0, 1 or 2;

R^8, $R^{8'}$ are each independently selected from hydrogen or alkyl;

R^1 is alkyl;

R^2 is halogen;

R^3 is halogen;

n is 0 or 1; and

R^4 is hydrogen; or

a pharmaceutically acceptable salt thereof.

27. The compound according to claim 26 which is selected from 3-(2-bromo-6-fluoro-phenyl)-7-(3,3-dioxo-2,3-dihydro-3lambda*6*-benzo[1,3]oxathiol-5-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one, and 3-(2-bromo-phenyl)-7-(3,3-dioxo-2,3-dihydro-3lambda*6*-benzo[1,3]oxathiol-5-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one.

28. The compound of claim 2, wherein

A is A-6,

R^5 is hydrogen;

R^1 is alkyl;

R^2 is halogen;

R^3 is halogen;

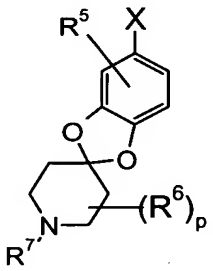
n is 0 or 1; and

R^4 is hydrogen; or

a pharmaceutically acceptable salt thereof.

29. The compound according to claim 28 which is selected from
3-(2-Bromo-5-methoxy-phenyl)-7-(4,4-dioxo-3,4-dihydro-2H-4lambda*6*-benzo[1,4]oxathiin-6-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
7-(4,4-Dioxo-3,4-dihydro-2H-4lambda*6*-benzo[1,4]oxathiin-6-ylamino)-3-(2-fluoro-6-methoxy-phenyl)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one,
3-(2-Bromo-phenyl)-7-(4,4-dioxo-3,4-dihydro-2H-4lambda*6*-benzo[1,4]oxathiin-6-ylamino)-1,4-dimethyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one; enantiomer 1,
3-(2-Bromo-phenyl)-7-(4,4-dioxo-3,4-dihydro-2H-4lambda*6*-benzo[1,4]oxathiin-6-ylamino)-1,4-dimethyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one; enantiomer 2,
3-(2-Bromo-phenyl)-1,4-dimethyl-7-(4-methyl-1,1,3-trioxo-1,2,3,4-tetrahydro-1lambda*6*-benzo[1,4]thiazin-7-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one; enantiomer 2,
3-(2-Bromo-phenyl)-1,4-dimethyl-7-(4-methyl-1,1,3-trioxo-1,2,3,4-tetrahydro-1lambda*6*-benzo[1,4]thiazin-7-ylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one; enantiomer 1, and
2-[7-(4,4-Dioxo-3,4-dihydro-2H-4lambda*6*-benzo[1,4]oxathiin-6-ylamino)-1-methyl-2-oxo-1,4-dihydro-2H-pyrimido[4,5-d]pyrimidin-3-yl]-3-fluoro-benzonitrile.

30. A compound of the formula A-1-I,



A-1-I

wherein

R^5 is hydrogen, halogen, hydroxy, cyano, amino, acylamino, alkyl, alkoxy, alkoxyalkyl, $-CONH_2$, $-SO_2NH_2$, $-S(O)_m$-alkyl, -NH-alkyl, $-N(alkyl)_2$, -CONH(alkyl), $-CON(alkyl)_2$, $-SO_2NH(alkyl)$ or $-SO_2N(alkyl)_2$;

R^6 each R^6 is independently selected from hydrogen, alkyl or oxo;

R^7 is hydrogen, acyl, alkoxycarbonyl, alkoxyalkyl, alkyl or

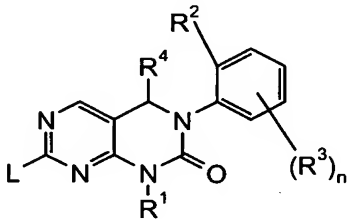
alkyl substituted with hydroxy, cyano,-$S(O)_m$-alkyl, amino, -NH-alkyl or -$N(alkyl)_2$;

m is 0, 1 or 2;

p is 0, 1 or 2; and

X is NO_2 or an optionally protected NH_2 group.

31. A process for the preparation of a compound of formula I comprising reacting a compound of the general formula



(II)

wherein

R^1 represents hydrogen or

alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl, or heteroarylalkyl, each of which may be optionally substituted with halogen, hydroxy, cyano, nitro, amino, acylamino, alkyl, alkoxy, alkoxyalkyl, -$CONH_2$, -SO_2NH_2, -$S(O)_m$-alkyl, -NH-alkyl, -$N(alkyl)_2$, -CONH(alkyl), $CON(alkyl)_2$, -$SO_2NH(alkyl)$, or -$SO_2N(alkyl)_2$;

R^2 represents halogen, cyano or CF_3;

R^3 each R^3 is independently selected from halogen, hydroxy, cyano, nitro, amino, acylamino, -$CONH_2$, -SO_2NH_2, -$S(O)_m$-alkyl, -NH-alkyl, -$N(alkyl)_2$, -CONH(alkyl), -$CON(alkyl)_2$, -$SO_2NH(alkyl)$, -$SO_2N(alkyl)_2$, or

alkyl, alkoxy or alkoxyalkyl, each of which may be optionally substituted with halogen, hydroxy, cyano, nitro, amino, acylamino, alkyl, alkoxy, alkoxyalkyl, -$CONH_2$, -SO_2NH_2, -$S(O)_m$-alkyl, -NH-alkyl, -$N(alkyl)_2$, -CONH(alkyl), $CON(alkyl)_2$, -$SO_2NH(alkyl)$, or -$SO_2N(alkyl)_2$;

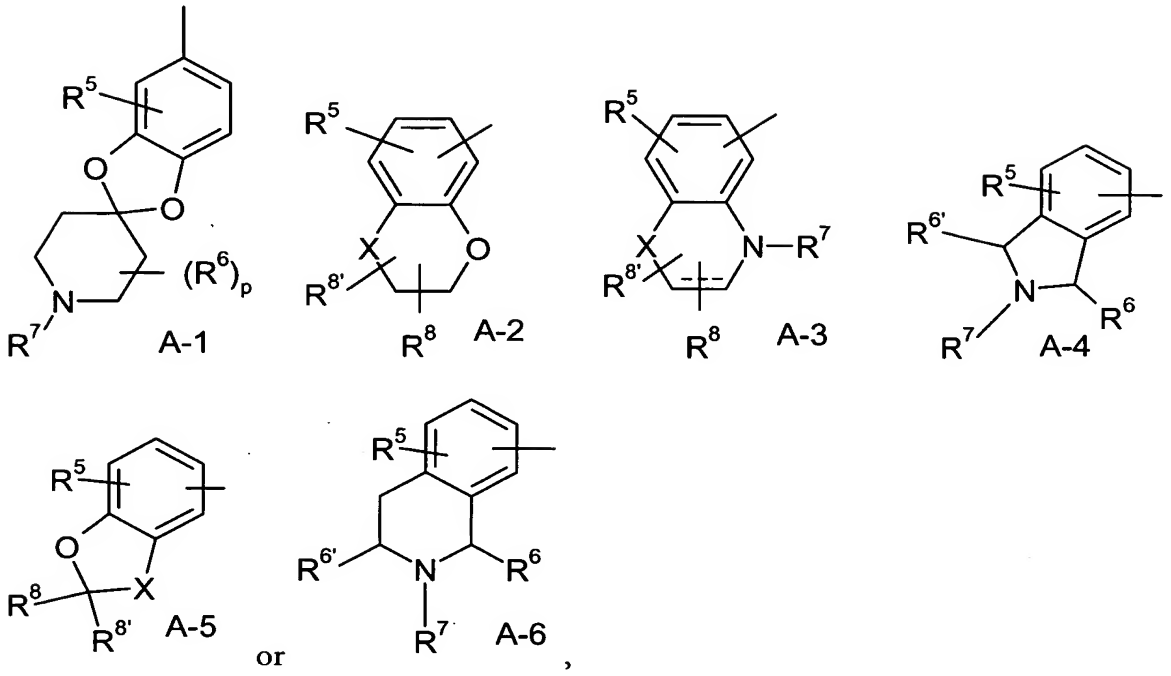
R^4 represents hydrogen, alkyl, alkoxy or cyano; and

L signifies a leaving group;

with an amine of the general formula

(III)

wherein A is selected from



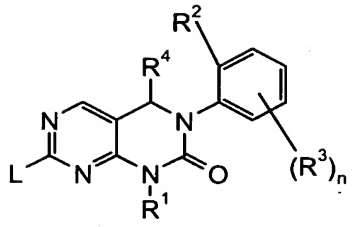
and R^5, R^6, $R^{6'}$, R^7, R^8, $R^{8'}$ and p have the meanings given in claim 2.

32. The process of claim 31 wherein the leaving group is selected from benzylsulphonyl, phenylsulphonyl, alkanesulphonyl, p-tolylsulfonyloxy, methanesulfonyloxy, trifluoromethanesulfonyloxy, chloro, bromo, iodo, or fluoro.

33. The process of claim 31 further comprising deprotecting a protected hydroxy or protected amino group present in the reaction product.

34. A process for the preparation of a compound of formula I, comprising

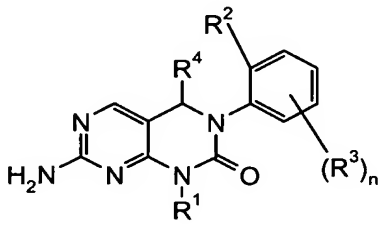
(a) reacting a compound of formula II



II

with ammonia or a protected amine;

(b) cleaving the protecting group L to give a compound of formula (IV);



(IV)

and

(c) reacting the compound of formula (IV) with a bicyclic compound of formula

(V)

wherein, in the above formulas

R^1 represents hydrogen or

alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl, or heteroarylalkyl, each of which may be optionally substituted with halogen, hydroxy, cyano, nitro, amino, acylamino, alkyl, alkoxy, alkoxyalkyl, $-CONH_2$, $-SO_2NH_2$, $-S(O)_m$-alkyl, -NH-alkyl, $-N(alkyl)_2$, -CONH(alkyl), $CON(alkyl)_2$, $-SO_2NH(alkyl)$, or $-SO_2N(alkyl)_2$;

R^2 represents halogen, cyano or CF_3;

R^3 each R^3 is independently selected from halogen, hydroxy, cyano, nitro, amino, acylamino, $-CONH_2$, $-SO_2NH_2$, $-S(O)_m$-alkyl, -NH-alkyl, $-N(alkyl)_2$, -CONH(alkyl), $-CON(alkyl)_2$, $-SO_2NH(alkyl)$, $-SO_2N(alkyl)_2$, or

alkyl, alkoxy or alkoxyalkyl, each of which may be optionally substituted with halogen, hydroxy, cyano, nitro, amino, acylamino, alkyl, alkoxy, alkoxyalkyl, $-CONH_2$, $-SO_2NH_2$, $-S(O)_m$-alkyl, -NH-alkyl, $-N(alkyl)_2$, -CONH(alkyl), $CON(alkyl)_2$, $-SO_2NH(alkyl)$, or $-SO_2N(alkyl)_2$;

R^4 represents hydrogen, alkyl, alkoxy or cyano;

n is 0, 1 or 2;

m is 0, 1 or 2;

L and L' represent a leaving group; and

A has the meaning given in claim 2.

35. The process of claim 34 wherein the cleaving group L' is chloro, iodo, p-tolylsulfonyloxy, methanesulfonyloxy, or trifluoromethanesulfonyloxy.

36. The process of claim 34 wherein the reaction of Compound (IV) with Compound (V) may be catalysed by a transition metal catalyst.

37. The process of claim 34 further comprisingconverting a basic compound of formula I synthesis into a pharmaceutically acceptable salt using an acid, or converting an acidic compound of formula I into a pharmaceutically acceptable salt using a base.

38. The process of claim 34 further comprisingconverting the resulting compound of formula I into a N-oxide by oxidation with an oxidizing agent.

39. The process of claim 38 wherein the oxidizing agent is selected from 3-chloro-perbenzoic acid, trifluoroperacetic acid, or dimethyldioxiran.

40. A pharmaceutical composition comprising a compound of formula I and a pharmaceutically acceptable adjuvant.

41. A method of treating an inflammatory-, immunological- or CNS disorders comprising administering to a patient in need of such treatment a therapeutically effective amount of at least one compound of claim 1.

42. A method of treating bone disease comprising administering to a patient in need of such treatment a therapeutically effective amount of at least one compound of claim 1.

43. A method of treating cancer comprising administering to a patient in need of such treatment a therapeutically effective amount of at least one compound of claim 1.